

Supporting Information

**Small Molecule Inhibitors of Regulator of G Protein Signalling
(RGS) Proteins**

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Contents:

- a. Tabulated pharmacological data for all final compounds
- b. Experimental details, including spectra for all compounds.

Table 1:

#	R1	R2	RGS4	RGS8	Selectivity
			IC50 (nM)	IC50 (μM)	RGS4/ RGS8
1a	4-FBn	4-MePh	30.1	11.0	366
1b	4-FBn	Ph	16.3	6.2	380
1c	4-FBn	4-CIPh	13.5	7.6	564
1d	4-FBn	4-MeOPh	10.9	11.4	1050
1e	4-FBn	3,4-diCIPh	35.7	17.2	481
1f	4-FBn	3-CF ₃ Ph	79.3	16.2	204
1g	4-FBn	3-MePh	121	7.1	59
1h	4-FBn	3-CIPh	52.3	12.8	245
1i	4-FBn	4-MeBn	12.9	39.8	3090
S1	4-FBn	4-t-BuPh	21.5	20.4	949
S2	4-FBn	4-Me ₂ NPh	146	10.3	71
2a	Bn	4-MePh	14.4	7.5	519
2b	Bn	Ph	23.5	5.6	239
2c	Bn	4-CIPh	28.7	5.2	183
2d	Bn	4-MeOPh	23.9	12.3	515
2e	Bn	3,4-diCIPh	88.9	13.2	149
2f	Bn	3-CF ₃ Ph	57.4	16.4	286
2g	Bn	3-MePh	38.2	21.3	558
2h	Bn	3-CIPh	32.5	10.9	335
2i	Bn	4-MeBn	7.2	20.4	2840
S3	Bn	4-t-BuPh	44.0	17.4	395
3	4-ClBn	4-MePh	5.4	11.8	2170
S4	4-ClBn	Ph	9.9	7.5	754
S5	4-ClBn	4-CIPh	25.8	12.7	492
S6	4-ClBn	4-MeOPh	166	40.2	241
S7	4-ClBn	3,4-diCIPh	155	43.2	279
S8	4-ClBn	4-MeBn	73.4	337	459
4	4-MeBn	4-MePh	8.6	11.6	1340
S9	4-MeBn	Ph	8.8	8.3	938
S10	4-MeBn	4-CIPh	16.9	12.8	757
S11	4-MeBn	4-MeOPh	10.9	6.6	607
S12	4-MeBn	3,4-diCIPh	82.5	175	2120
S13	4-MeBn	4-MeBn	32.8	94.7	2890
5	3-ClBn	4-MePh	17.4	17.5	1005
S14	3-ClBn	Ph	30.7	9.4	306
S15	3-ClBn	4-t-BuPh	224	32.2	144
S16	3-ClBn	3-MePh	64.5	10.1	156
S17	3-ClBn	3-CIPh	419	21.1	50
S18	3-ClBn	3-CF ₃ Ph	1440	16.2	11
6	3-MeBn	4-MePh	14.5	9.9	679
S19	3-MeBn	Ph	15.1	8.4	555
S20	3-MeBn	4-t-BuPh	191	17.8	93
S21	3-MeBn	3-MePh	45.6	10.4	228
S22	3-MeBn	3-CIPh	381	31.0	82
S23	3-MeBn	3-CF ₃ Ph	N/A	15.9	N/A
7	4-MeOBn	4-MePh	176	312	1780
S24	4-MeOBn	Ph	33.7	7.2	214
S25	4-MeOBn	4-CIPh	68.7	9.9	144
S26	4-MeOBn	4-MeOPh	35.2	17.6	500

S27	4-MeOBn	3,4-diClPh	87.4	36.0	412
S28	4-MeOBn	4-MeBn	103	92.9	901
8	3,4-diClBn	4-MePh	34.2	15.7	460
S29	3,4-diClBn	Ph	24.1	7.5	313
S30	3,4-diClBn	4-CIPh	68.4	16.7	244
S31	3,4-diClBn	4-MeOPh	12.8	5.9	464
S32	3,4-diClBn	3,4-diClPh	155	125	805
S33	3,4-diClBn	4-MeBn	113	109	962
S34	4-t-BuBn	4-MePh	178	>100	N/A
S35	4-t-BuBn	Ph	246	>100	N/A
S36	4-t-BuBn	4-t-BuPh	351	>100	N/A
9a	4-FBn	n-Bu	15.6	31.6	2020
9b	4-FBn	Et	22.3	18.7	842
10a	Me	4-MePh	18.9	8.4	445
10b	Me	Et	22.3	37.0	1660
10c	Me	n-Bu	23.5	28.4	1210
10d	Me	t-Bu	27.8	56.0	2020
11a	n-Bu	4-MePh	19.7	9.5	483
11b	n-Bu	Et	14.4	83.5	5810
11c	n-Bu	n-Bu	29.8	122	4110
11d	n-Bu	t-Bu	53.6	119	2220
12a	i-Bu	4-MePh	14.0	7.7	550
12b	i-Bu	Et	26.3	70.6	2680
12c	i-Bu	n-Bu	38.6	98.0	2540
12d	i-Bu	t-Bu	29.1	194	6660
13	MeOCH ₂ CH ₂	Et	54.3	36.1	665
14	4-MeBn*	4-MePh*	>100000	>100	N/A
15	Bn**	4-MePh**	93300	0.0	0
S37	Bn**	Br**	32900	144	4

^aValues are an average from two independent experiments. * Scheme 2 for structure of **14** ** Scheme 3 for structure of **15**

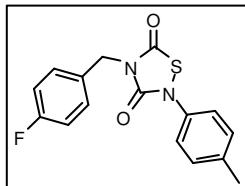
Supplementary Information

General Procedures:

All reactions were carried out under an inert atmosphere of nitrogen with dry solvents, using anhydrous conditions unless otherwise stated. Dry tetrahydrofuran (THF) was distilled from the sodium benzophenone ketyl radical. Reagents were purchased at the highest commercial quality and used without further purification. Column chromatography was performed with a Combiflash Rf Companion, using Redisep Rf disposable columns containing 40-60 µm silica, using reagent grade ethyl acetate and petroleum ether. A Bruker Avance III 400 MHz NMR spectrometer was used to record ¹H and ¹³C NMR spectra. Microanalysis for key compounds was determined with a Perkin Elmer 240C analyser.

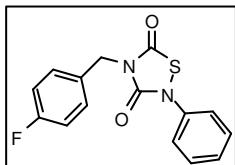
General Procedure for synthesis of 1,2,4-thiadiazolidine-3,5-diones:

A stirred solution of isocyanate (1 mmol) and isothiocyanate (1 mmol) in THF (5 mL) was cooled to 0 °C. Sulfuryl chloride (1 mmol) was added slowly (either as straight or as a 1 M solution in CH₂Cl₂) and the mixture was allowed to warm to room temperature and stirred overnight. The reaction was then opened to the air and stirred for 30 minutes before the solvent was removed under reduced pressure. Flash chromatography (0-20% ethyl acetate in pet ether) was used to purify the crude reaction mixture.



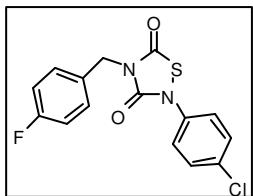
2-p-tolyl-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1a):

Yield = 41 %. ¹H NMR (400 MHz, CDCl₃) δ 2.35 (s, 3H), 4.87 (s, 2H), 7.01-7.05 (m, 2H), 7.20-7.22 (m, 2H), 7.35-7.38 (m, 2H), 7.48-7.51 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 20.9, 45.3, 115.6 (d, *J*_{CF} = 21.6 Hz), 123.7, 130.0, 130.9 (d, *J*_{CF} = 3.3 Hz), 131.1, (d, *J*_{CF} = 8.3 Hz), 133.0, 137.3, 151.0, 162.7 (d, *J*_{CF} = 247.4 Hz), 165.1; anal. (C₁₆H₁₃FN₂O₂S); CHN



2-phenyl-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1b):

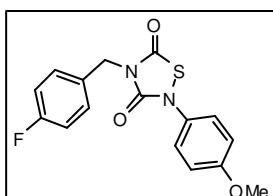
Yield = 68 %. ¹H NMR (400 MHz, CDCl₃) δ 4.88 (s, 2H), 7.04 (t, *J* = 8.6 Hz, 2H), 7.26-7.30 (m, 1H), 7.40-7.44 (m, 2H), 7.48-7.51 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 45.4, 115.7 (d, *J*_{CF} = 21.5 Hz), 123.4, 127.1, 129.5, 130.9 (d, *J*_{CF} = 3.1 Hz), 131.1 (d, *J*_{CF} = 7.6 Hz), 135.7, 150.9, 162.7 (d, *J*_{CF} = 246.9 Hz), 165.0.



2-(4-chlorophenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione

(1c):

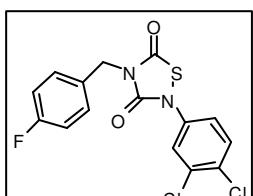
Yield = 64 %. ^1H NMR (400 MHz, CDCl_3) δ 4.87 (s, 2H), 7.04 (t, J = 8.6 Hz, 2H), 7.37-7.40 (m, 2H), 7.44-7.50 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.5, 115.7 (d, J_{CF} = 21.4 Hz), 124.5, 129.6, 130.7 (d, J_{CF} = 3.9 Hz), 131.2 (d, J_{CF} = 8.4 Hz), 132.6, 134.2, 150.8, 162.8 (d, J_{CF} = 247.6 Hz), 164.5.



2-(4-methoxyphenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione

(1d):

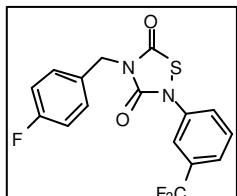
Yield = 71 %. ^1H NMR (400 MHz, CDCl_3) δ 3.81 (s, 3H), 4.86 (s, 2H), 6.91-6.93 (m, 2H), 7.01-7.05 (m, 2H), 7.36-7.38 (m, 2H), 7.48-7.51 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.4, 55.6, 114.8, 115.7 (d, J_{CF} = 22.1 Hz), 126.2, 128.0, 131.0 (d, J_{CF} = 3.0 Hz), 131.1 (d, J_{CF} = 8.0 Hz), 151.4, 158.9, 162.8 (d, J_{CF} = 246.4 Hz), 165.3.



2-(3,4-dichlorophenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione

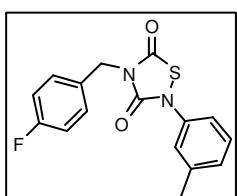
(1e):

Yield = 52 %. ^1H NMR (400 MHz, CDCl_3) δ 4.87 (s, 2H), 7.04 (t, J = 8.6 Hz, 2H), 7.34-7.36 (m, 1H), 7.46-7.50 (m, 3H), 7.70-7.71 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.6, 115.8 (d, J_{CF} = 21.5 Hz), 122.0, 124.8, 130.5 (d, J_{CF} = 3.0 Hz), 130.8, 131.0, 131.2 (d, J_{CF} = 8.4 Hz), 133.6, 135.1, 150.7, 162.8 (d, J_{CF} = 247.6 Hz).



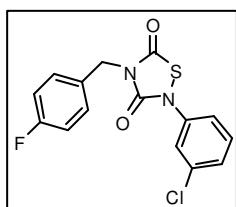
2-(3-trifluoromethylphenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1f):

Yield = 65 %. ^1H NMR (400 MHz, CDCl_3) δ 4.89 (s, 2H), 7.02-7.07 (m, 2H), 7.48-7.51 (m, 2H), 7.54-7.55 (m, 2H), 7.67-7.70 (m, 1H), 7.84-7.85 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.6, 115.8 (d, J_{CF} = 22.1 Hz), 120.0 (q, J_{CF} = 4.0 Hz), 123.4 (q, J_{CF} = 272.6 Hz), 123.5 (q, J_{CF} = 3.0 Hz), 126.1, 130.2, 130.6 (d, J_{CF} = 3.0 Hz), 131.2 (d, J_{CF} = 8.0 Hz), 132.2 (d, J_{CF} = 33.2 Hz), 136.5, 150.9, 162.9 (d, J_{CF} = 247.5 Hz), 164.2.



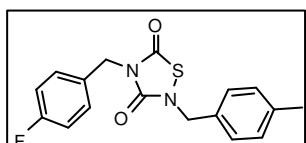
2-(3-methylphenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1g):

Yield = 72 %. ^1H NMR (400 MHz, CDCl_3) δ 2.38 (s, 3H), 4.87 (s, 2H), 7.02-7.06 (m, 2H), 7.08-7.11 (m, 1H), 7.28-7.30 (m, 2H), 7.31-7.33 (m, 1H), 7.48-7.51 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 45.4, 115.7 (d, J_{CF} = 21.6 Hz), 120.6, 124.2, 128.0, 129.3, 131.0 (d, J_{CF} = 3.2 Hz), 131.1 (d, J_{CF} = 8.2 Hz), 135.6, 139.8, 151.0, 162.8 (d, J_{CF} = 247.3 Hz), 165.1.



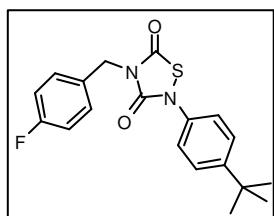
2-(3-chlorophenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1h):

Yield = 60 %. ^1H NMR (400 MHz, CDCl_3) δ 4.88 (s, 2H), 7.02-7.06 (m, 2H), 7.24-7.27 (m, 1H), 7.32-7.39 (m, 2H), 7.47-7.51 (m, 2H), 7.60-7.61 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.5, 115.8 (d, $J_{\text{CF}} = 21.6$ Hz), 121.0, 123.3, 127.0, 130.4, 130.7 (d, $J_{\text{CF}} = 24.5$ Hz), 131.2 (d, $J_{\text{CF}} = 8.3$ Hz), 135.3, 136.9, 150.8, 162.8 (d, $J_{\text{CF}} = 247.6$ Hz), 164.4.



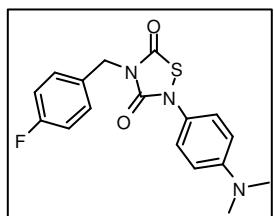
2-(4-methylbenzyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (1i):

Yield = 62 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.72 (s, 2H), 4.80 (s, 2H), 7.02 (t $J = 6.7$ Hz, 2H), 7.18 (s, 4H), 7.43-7.47 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 45.2, 48.6, 115.6 (d, $J_{\text{CF}} = 21.1$ Hz), 128.5, 129.7, 130.9 (d, $J_{\text{CF}} = 8.0$ Hz), 131.1 (d, $J_{\text{CF}} = 3.0$ Hz), 131.3, 138.9, 152.9, 162.7 (d, $J_{\text{CF}} = 247.5$ Hz), 165.9.



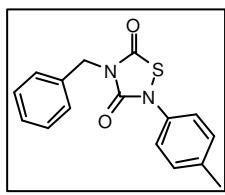
2-(4-t-butylphenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S1):

Yield = 81 %. ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 9H), 4.87 (s, 2H), 7.01-7.05 (m, 2H), 7.39-7.44 (m, 4H), 7.48-7.51 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 31.2, 34.7, 45.4, 115.7 (d, $J_{\text{CF}} = 21.6$ Hz), 123.5, 126.5, 131.0 (d, $J_{\text{CF}} = 3.2$ Hz), 131.2 (d, $J_{\text{CF}} = 8.2$ Hz), 132.9, 150.6, 151.1, 162.8 (d, $J_{\text{CF}} = 247.3$ Hz), 165.2.



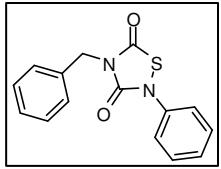
2-(4-dimethylaminophenyl)-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S2):

Yield = 35 %. ^1H NMR (400 MHz, CDCl_3) δ 2.83 (s, 6H), 4.90 (s, 2H), 7.03-7.09 (m, 4H), 7.27-7.32 (m, 1H), 7.46-7.51 (m, 3H).



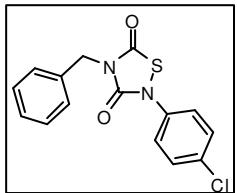
2-p-tolyl-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2a):

Yield = 88 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.91 (s, 2H), 7.20 (d, $J = 8.6$ Hz, 2H), 7.26-7.38 (m, 5H), 7.51 (d, $J = 6.2$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 46.1, 123.6, 128.3, 128.7, 129.1, 130.0, 133.0, 135.0, 137.2, 151.1, 165.2.



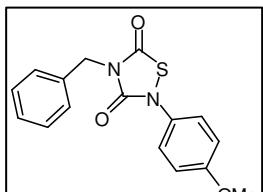
2-phenyl-4-benzyl-1,2,4-thiadiazoline-3,5-dione (2b):

Yield = 81 %. ^1H NMR (400 MHz, CDCl_3) δ 4.92 (s, 2H), 7.26-7.30 (m, 1H), 7.33-7.39 (m, 4H), 7.41-7.43 (m, 1H), 7.50-7.52 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 46.1, 123.4, 126.9, 128.4, 128.8, 129.1, 129.5, 135.0, 135.8, 150.9, 165.0.



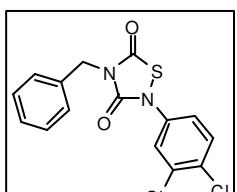
2-(4-chlorophenyl)-4-benzyl-1,2,4-thiazolidine-3,5-dione (2c):

Yield = 60 %. ^1H NMR (400 MHz, CDCl_3) δ 4.91 (s, 2H), 7.33-7.39 (m, 5H), 7.44-7.51 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 46.3, 124.5, 128.8, 129.1, 129.6, 132.5, 134.5, 134.9, 150.9, 164.5



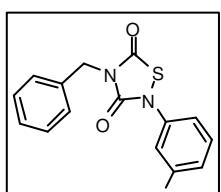
2-(4-methoxyphenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2d):

Yield = 58 %. ^1H NMR (400 MHz, CDCl_3) δ 3.81 (s, 3H), 4.90 (s, 2H), 6.92 (d, $J = 9.0$ Hz, 2H), 7.32-7.39 (m, 5H), 7.49-7.52 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 46.2, 55.6, 114.7, 126.2, 128.1, 128.3, 128.7, 129.1, 135.1, 151.4, 158.8, 165.3.



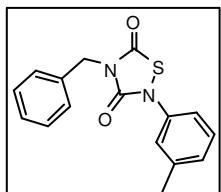
2-(3,4-dichlorophenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2e):

Yield = 55 %. ^1H NMR (400 MHz, CDCl_3) δ 4.91 (s, 2H), 7.33-7.38 (m, 4H), 7.46-7.50 (m, 3H), 7.72 (d, $J = 2.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 46.2, 121.9, 124.7, 128.5, 128.8, 129.1, 130.6, 130.9, 133.5, 134.6, 135.2, 150.7, 164.0.



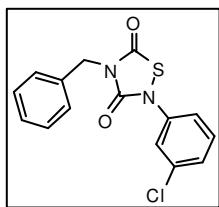
2-(3-trifluoromethylphenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2f):

Yield = 57 %. ^1H NMR (400 MHz, CDCl_3) δ 4.93 (s, 2H), 7.34-7.39 (m, 3H), 7.49-7.57 (m, 4H), 7.68-7.71 (m, 1H), 7.85-7.86 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 46.3, 119.8 (q, $J_{\text{CF}} = 3.7$ Hz), 123.2 (q, $J_{\text{CF}} = 3.7$ Hz), 123.3 (q, $J_{\text{CF}} = 272.6$ Hz), 125.9 (app. d, $J_{\text{CF}} = 0.9$ Hz), 128.5, 128.8, 129.1, 130.1, 132.0 (q, $J_{\text{CF}} = 33.1$ Hz), 134.7, 136.5, 150.9, 164.2.



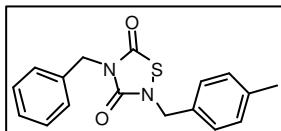
2-(3-methylphenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2g):

Yield = 59 %. ^1H NMR (400 MHz, CDCl_3) δ 2.37 (s, 3H), 4.91 (s, 2H), 7.07-7.10 (m, 1H), 7.28-7.29 (m, 2H), 7.32-7.38 (m, 4H), 7.49-7.52 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 46.2, 120.6, 124.1, 127.9, 128.4, 128.8, 129.1, 129.3, 135.1, 135.7, 139.7, 151.0, 165.2.



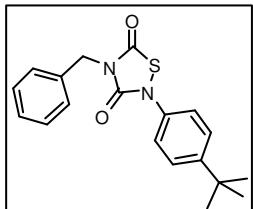
2-(3-chlorophenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2h):

Yield = 71 %. ^1H NMR (400 MHz, CDCl_3) δ 4.91 (s, 2H), 7.23-7.26 (m, 1H), 7.31-7.40 (m, 5H), 7.49-7.51 (m, 2H), 7.61-7.62 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 46.3, 120.9, 123.3, 126.9, 128.5, 128.9, 129.1, 130.4, 134.8, 135.3, 137.0, 150.8, 164.4.



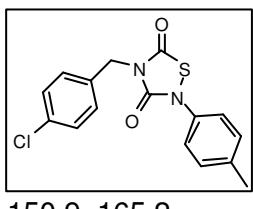
2-(4-methylbenzyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (2i):

Yield = 59 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.73 (s, 2H), 4.84 (s, 2H), 7.18 (app. s, 4H), 7.31-7.37 (m, 3H), 7.44-7.46 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 45.9, 48.6, 128.3, 128.6, 128.7, 128.9, 129.7, 131.4, 135.2, 138.8, 153.1, 165.9.



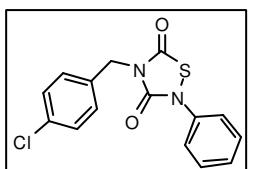
2-(4-t-butylphenyl)-4-benzyl-1,2,4-thiadiazolidine-3,5-dione (S3):

Yield = 79 %. ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 9H), 4.91 (s, 2H), 7.32-7.38 (m, 3H), 7.42 (app. s, 4H), 7.49-7.52 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 31.2, 34.7, 46.2, 123.4, 126.5, 128.4, 128.8, 129.1, 133.0, 135.1, 150.5, 151.2, 165.2.



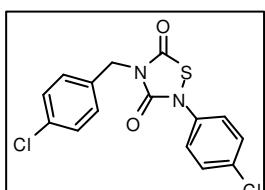
2-p-tolyl-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (3):

Yield = 84 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.86 (s, 2H), 7.20-7.22 (m, 2H), 7.31-7.37 (m, 4H), 7.43-7.45 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 45.4, 123.7, 128.9, 130.1, 130.6, 132.9, 133.5, 134.4, 137.4, 150.9, 165.2.



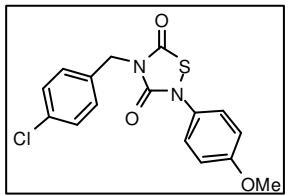
2-phenyl-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S4):

Yield = 61 %. ^1H NMR (400 MHz, CDCl_3) δ 4.87 (s, 2H), 7.26-7.33 (m, 3H), 7.40-7.49 (m, 4H), 7.49-7.51 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.4, 123.4, 127.1, 129.0, 129.5, 130.6, 133.4, 134.5, 135.6, 150.8, 165.0.



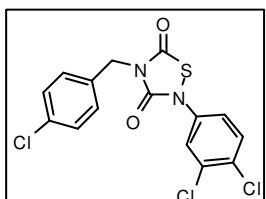
2-(4-chlorophenyl)-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S5):

Yield = 69 %. ^1H NMR (400 MHz, CDCl_3) δ 4.86 (s, 2H), 7.31-7.33 (m, 2H), 7.37-7.39 (m, 2H), 7.43-7.46 (m, 4H). ^{13}C NMR (100 Hz, CDCl_3) δ 45.5, 124.5, 128.8, 129.0, 129.03, 129.96, 130.6, 132.6, 133.3, 134.2, 134.6, 150.8, 164.5.



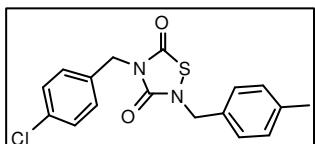
2-(4-methoxyphenyl)-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S6):

Yield = 25 %. ^1H NMR (400 MHz, CDCl_3) δ 3.81 (s, 3H), 4.86 (s, 2H), 6.91-6.93 (m, 2H), 7.31-7.33 (m, 2H), 7.35-7.38 (m, 2H), 7.43-7.45 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.4, 55.5, 114.2, 114.7, 126.2, 127.9, 128.9, 130.6, 133.5, 134.4, 151.3, 158.9, 165.3.



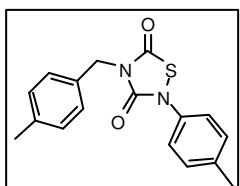
2-(3,4-dichlorophenyl)-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S7):

Yield = 37 %. ^1H NMR (400 MHz, CDCl_3) δ 4.87 (s, 2H), 7.32-7.36 (m, 3H), 7.42-7.49 (m, 3H), 7.70 (d, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.6, 122.0, 124.8, 129.1, 130.6, 130.9, 131.0, 133.1, 133.6, 134.7, 135.1, 150.7.



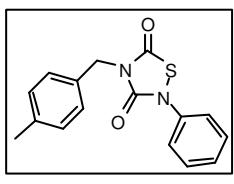
2-(4-methylbenzyl)-4-(4-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S8):

Yield = 69 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.72 (s, 2H), 4.79 (s, 2H), 7.17 (app. s, 4H), 7.30-7.32 (m, 2H), 7.38-7.40 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.1, 45.2, 48.5, 128.5, 128.9, 129.7, 130.3, 131.2, 133.6, 134.3, 138.9, 152.8, 165.8.



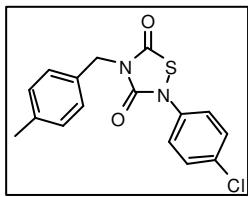
2-p-tolyl-4-(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (4):

Yield = 74 %. ^1H NMR (400 MHz, CDCl_3) δ 2.34 (s, 3H), 2.35 (s, 3H), 4.87 (s, 2H), 7.15-7.21 (m, 4H), 7.35-7.41 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 21.2, 45.9, 123.7, 129.1, 129.4, 130.0, 132.2, 133.2, 137.2, 138.2, 151.1, 165.2.



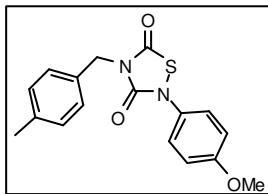
2-phenyl-4-(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S9):

Yield = 74 %. ^1H NMR (400 MHz, CDCl_3) δ 2.34 (s, 3H), 4.88 (s, 2H), 7.16 (d, J = 7.8 Hz, 2H), 7.25-7.29 (m, 1H), 7.39-7.43 (m, 4H), 7.50 (d, J = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 45.9, 123.4, 126.9, 129.1, 129.4, 129.5, 132.1, 135.8, 138.2, 151.0, 165.0.



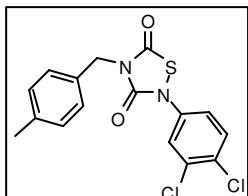
**2-(4-chlorophenyl)-4-(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione
(S10):**

Yield = 80 %. ^1H NMR (400 MHz, CDCl_3) δ 2.34 (s, 3H), 4.87 (s, 2H), 7.16 (d, J = 7.8 Hz, 2H), 7.35-7.40 (m, 4H), 7.44-7.46 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 46.0, 124.5, 129.1, 129.4, 129.5, 131.9, 132.4, 134.4, 138.4, 150.9, 164.5.



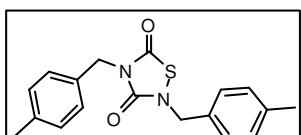
**2-(4-methoxyphenyl)-4-(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione
(S11):**

Yield = 69 %. ^1H NMR (400 MHz, CDCl_3) δ 2.34 (s, 3H), 3.81 (s, 3H), 4.87 (s, 2H), 6.91-6.93 (m, 2H), 7.16 (d, J = 7.9 Hz, 2H), 7.36-7.41 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.1, 45.9, 55.5, 114.7, 126.1, 128.1, 129.1, 129.4, 132.2, 138.2, 151.4, 158.8, 165.3.



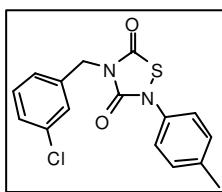
**2-(3,4-dichlorophenyl)-4-(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione
(S12):**

Yield = 67 %. ^1H NMR (400 MHz, CDCl_3) δ 2.34 (s, 3H), 4.87 (s, 2H), 7.17 (d, J = 7.8 Hz, 2H), 7.35 (dd, J = 2.6, 8.8 Hz, 1H), 7.36 (m, 2H), 7.46 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.2, 46.1, 121.9, 124.7, 129.1, 129.5, 130.6, 130.9, 131.7, 133.5, 135.2, 138.5, 150.8, 164.1.



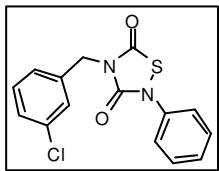
2,4-bis(4-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S13):

Yield = 78 %. ^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 3H), 2.35 (s, 3H), 4.71 (s, 2H), 4.80 (s, 2H), 7.13-7.15 (m, 2H), 7.17 (app. s, 4H), 7.34-7.36 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.10, 21.12, 45.7, 48.5, 128.5, 128.9, 129.3, 129.6, 131.4, 132.3, 138.0, 138.7, 153.0, 165.9.



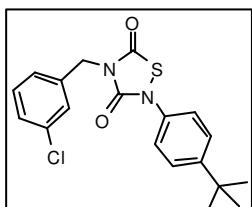
2-p-tolyl-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (5):

Yield = 68 %. ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 4.87 (s, 2H), 7.20-7.32 (m, 4H), 7.36-7.39 (m, 3H), 7.48-7.49 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 45.5, 123.7, 127.3, 128.7, 129.2, 129.6, 130.06, 130.10, 133.0, 134.6, 136.9, 137.4, 150.9, 165.2.



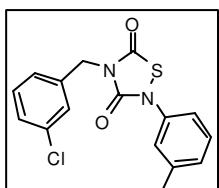
2-phenyl-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S14):

Yield = 88 %. ^1H NMR (400 MHz, CDCl_3) δ 4.88 (s, 2H), 7.29-7.31 (m, 3H), 7.38-7.44 (m, 3H), 7.49-7.53 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.5, 123.5, 127.1, 127.3, 128.7, 129.1, 129.2, 129.6, 130.1, 134.7, 135.7, 136.8, 150.8, 164.9.



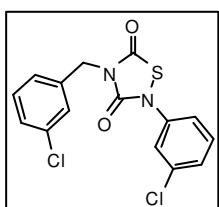
2-(4-t-butylphenyl)-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S15):

Yield = 72 %. ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 9H), 4.87 (s, 2H), 7.28-7.30 (m, 2H), 7.37-7.40 (m, 1H), 7.42-7.43 (m, 4H), 7.49-7.50 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 31.2, 34.7, 45.5, 123.5, 126.5, 127.3, 128.7, 129.2, 130.1, 132.9, 134.6, 136.9, 150.6, 150.9, 165.2.



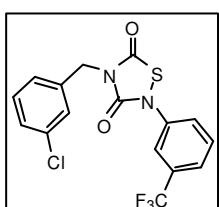
2-m-tolyl-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S16):

Yield = 59 %. ^1H NMR (400 MHz, CDCl_3) δ 2.38 (s, 3H), 4.87 (s, 2H), 7.08-7.11 (m, 1H), 7.26-7.30 (m, 4H), 7.31-7.33 (m, 1H), 7.37-7.39 (m, 1H), 7.48-7.49 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 45.5, 120.6, 124.2, 127.3, 128.0, 128.7, 129.2, 129.3, 130.1, 134.7, 135.6, 136.9, 139.8, 150.8, 165.1.



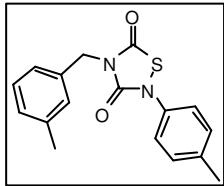
2-(3-chlorophenyl)-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S17):

Yield = 81 %. ^1H NMR (400 MHz, CDCl_3) δ 4.87 (s, 2H), 7.24-7.32 (m, 4H), 7.34-7.39 (m, 2H), 7.47-7.48 (m, 1H), 7.61-7.62 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.6, 121.0, 123.3, 127.1, 127.3, 128.8, 129.2, 130.1, 130.5, 134.7, 135.3, 136.6, 136.9, 150.7, 164.4.



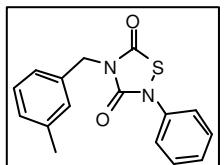
2-(3-trifluoromethylphenyl)-4-(3-chlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S18):

Yield = 67 %. ^1H NMR (400 MHz, CDCl_3) δ 4.88 (s, 2H), 7.27-7.33 (m, 2H), 7.37-7.42 (m, 1H), 7.48-7.49 (m, 1H), 7.54-7.58 (m, 2H), 7.69-7.71 (m, 1H), 7.84 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.7, 119.9 (q, $J_{\text{CF}} = 4.0$ Hz), 123.4 (q, $J_{\text{CF}} = 271.6$), 123.5 (q, $J_{\text{CF}} = 4.0$ Hz), 126.1, 127.3, 128.9, 129.2, 129.6, 130.2 (d, $J_{\text{CF}} = 3.0$ Hz), 132.2 (q, $J_{\text{CF}} = 33.2$ Hz), 134.7, 136.4, 136.5, 150.8, 164.2.



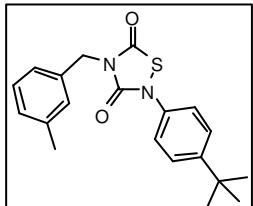
2-(4-methylphenyl)-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (6):

Yield = 78 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 6H), 4.87 (s, 2H), 7.13-7.14 (m, 1H), 7.19-7.24 (m, 3H), 7.29-7.31 (m, 2H), 7.36-7.38 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 21.4, 46.2, 123.7, 126.2, 128.7, 129.1, 129.8, 130.1, 133.2, 135.0, 137.2, 138.5, 151.2, 165.2.



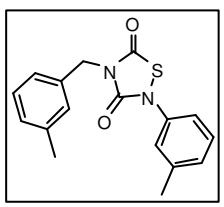
2-phenyl-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S19):

Yield = 76 %. ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 4.88 (s, 2H), 7.13-7.15 (m, 1H), 7.22-7.27 (m, 2H), 7.28-7.31 (m, 2H), 7.39-7.43 (m, 2H), 7.50-7.53 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 46.2, 123.4, 126.2, 127.0, 128.7, 129.2, 129.5, 129.8, 135.0, 135.9, 138.5, 151.0, 165.0.



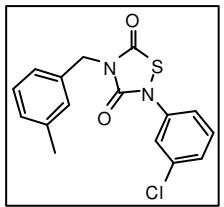
2-(4-t-butylphenyl)-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S20):

Yield = 70 %. ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 9H), 2.35 (s, 3H), 4.88 (s, 2H), 7.13 (br. d, J = 7.5 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.30-7.31 (m, 2H), 7.42 (app. d, J = 3.6 Hz, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 31.2, 34.6, 46.2, 123.4, 126.2, 126.4, 128.7, 129.1, 129.8, 133.1, 135.0, 138.5, 150.4, 151.2, 165.2.



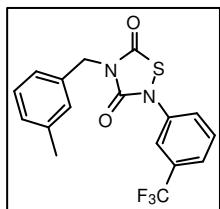
2-m-tolyl-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S21):

Yield = 89 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 2.37 (s, 3H), 4.87 (s, 2H), 7.07-7.09 (m, 1H), 7.12-7.14 (m, 1H), 7.22-7.24 (m, 1H), 7.28-7.30 (m, 4H), 7.33-7.34 (m 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 46.2, 120.5, 124.1, 126.2, 127.9, 128.7, 129.1, 129.3, 129.7, 135.0, 135.7, 138.5, 139.7, 151.1, 165.2.



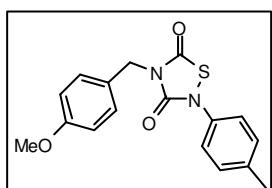
2-(3-chlorophenyl)-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S22):

Yield = 66 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 4.87 (s, 2H), 7.13-7.15 (m, 1H), 7.22-7.25 (m, 2H), 7.28-7.31 (m, 2H), 7.31-7.35 (m, 1H), 7.37-7.39 (m, 1H), 7.61-7.62 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.3, 46.2, 120.8, 123.2, 126.1, 126.8, 128.7, 129.2, 129.7, 130.3, 134.7, 135.2, 137.0, 138.5, 150.8, 164.4.



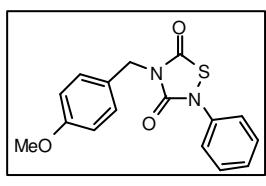
2-(3-trifluoromethylphenyl)-4-(3-methylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S23):

Yield = 87 %. ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 4.89 (s, 2H), 7.14-7.16 (m, 1H), 7.23-7.27 (m, 1H), 7.29-7.30 (m, 2H), 7.52-7.56 (m, 2H), 7.68-7.71 (m, 1H), 7.85 (br app. s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 46.4, 119.9 (q, $J_{\text{CF}} = 4.0$ Hz), 123.3 (q, $J_{\text{CF}} = 4.0$ Hz), 123.4 (q, $J_{\text{CF}} = 272.6$ Hz), 126.0, 126.2, 128.8, 129.3, 129.7, 130.1, 132.1 (q, $J_{\text{CF}} = 33.2$ Hz), 134.7, 136.6, 138.6, 151.0, 164.3.



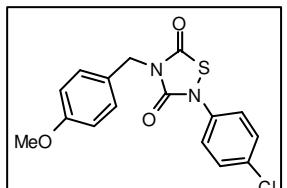
2-p-tolyl-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (7):

Yield = 65 %. ^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 3.80 (s, 3H), 4.85 (s, 2H), 6.86-6.88 (m, 2H), 7.19-7.21 (m, 2H), 7.35-7.37 (m, 2H), 7.44-7.46 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 45.6, 55.3, 114.1, 123.7, 127.4, 129.5, 130.0, 130.7, 133.1, 137.2, 151.1, 159.7, 165.2.



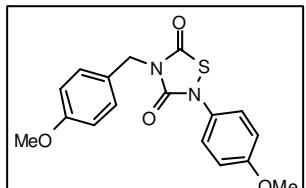
2-phenyl-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (S24):

Yield = 83 %. ^1H NMR (400 MHz, CDCl_3) δ 3.83 (s, 3H), 4.89 (s, 2H), 6.89-6.93 (m, 2H), 7.28-7.36 (m, 2H), 7.40-7.55 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.7, 55.3, 114.1, 123.4, 126.9, 127.3, 129.0, 129.5, 130.7, 135.8, 151.0, 159.7, 165.0.



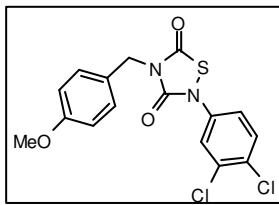
2-(4-chlorophenyl)-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (S25):

Yield = 77 %. ^1H NMR (400 MHz, CDCl_3) δ 3.79 (s, 3H), 4.84 (s, 2H), 6.86-6.88 (m, 2H), 7.36-7.38 (m, 2H), 7.43-7.46 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.8, 55.3, 114.1, 124.5, 127.1, 129.5, 130.7, 132.4, 134.4, 150.9, 159.7, 164.5.



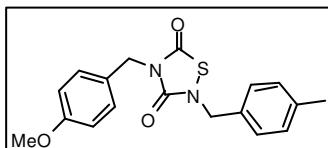
2-(4-methoxyphenyl)-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (S26):

Yield = 63 %. ^1H NMR (400 MHz, CDCl_3) δ 3.80 (s, 3H), 3.81 (s, 3H), 4.84 (s, 2H), 6.86-6.92 (m, 4H), 7.36-7.38 (m, 2H), 7.44-7.46 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 45.7, 55.2, 55.5, 114.0, 114.7, 126.1, 127.4, 128.1, 130.7, 151.5, 158.8, 159.7, 165.3.



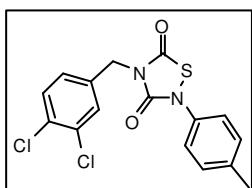
2-(3,4-dichlorophenyl)-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (S27):

Yield = 67 %. ¹H NMR (400 MHz, CDCl₃) δ 3.80 (s, 3H), 4.85 (s, 2H), 6.87-6.89 (m, 2H), 7.35 (dd, *J* = 2.6, 8.7 Hz, 1H), 7.42-7.47 (m, 3H), 7.71 (d, *J* = 2.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 45.9, 55.3, 114.2, 122.0, 124.8, 126.9, 130.7, 130.9, 133.5, 135.2, 150.8, 159.8, 164.1.



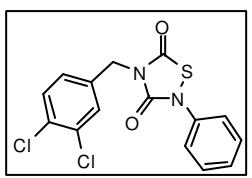
2-(4-methylbenzyl)-4-(4-methoxybenzyl)-1,2,4-thiadiazolidine-3,5-dione (S28):

Yield = 36 %. ¹H NMR (400 MHz, CDCl₃) δ 2.35 (s, 3H), 3.80 (s, 3H), 4.72 (s, 2H), 4.78 (s, 2H), 6.85-6.88 (m, 2H), 7.17 (s, 4H), 7.40-7.42 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 21.2, 45.5, 48.5, 55.3, 114.0, 127.5, 128.5, 129.7, 130.5, 131.4, 138.8, 153.1, 159.6, 166.0.



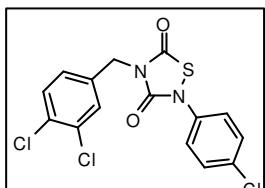
2-p-tolyl-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (8):

Yield = 72 %. ¹H NMR (400 MHz, CDCl₃) δ 2.39 (s, 3H), 4.87 (s, 2H), 7.24-7.29 (m, 2H), 7.36-7.41 (m, 3H), 7.45-7.47 (m, 1H), 7.63-7.64 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 44.9, 123.8, 128.6, 130.1, 130.8, 131.2, 132.8, 132.9, 135.1, 137.6, 150.9, 165.1.



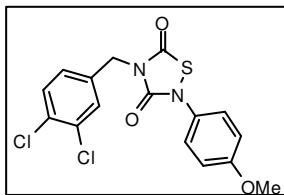
2-phenyl-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S29):

Yield = 78 %. ¹H NMR (400 MHz, CDCl₃) δ 4.85 (s, 2H), 7.28-7.32 (m, 1H), 7.34-7.36 (m, 1H), 7.41-7.44 (m, 3H), 7.49-7.52 (m, 2H), 7.60-7.61 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 44.9, 123.5, 127.2, 128.6, 129.6, 130.8, 131.1, 132.8, 132.9, 134.9, 135.6, 150.7, 164.9.



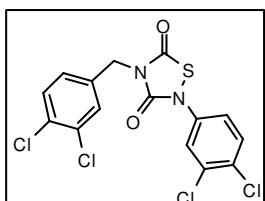
2-(4-chlorophenyl)-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S30):

Yield = 76 %. ¹H NMR (400 MHz, CDCl₃) δ 4.84 (s, 2H), 7.33 (dd, *J* = 2.0, 8.2 Hz, 1H), 7.38-7.42 (m, 3H), 7.44-7.47 (m, 2H), 7.59 (d, *J* = 2.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 45.0, 124.6, 128.6, 129.7, 130.8, 131.1, 132.8, 133.0, 134.1, 134.8, 150.7, 164.5.



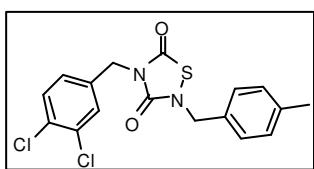
2-(4-methoxyphenyl)-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S31):

Yield = 80 %. ¹H NMR (400 MHz, CDCl₃) δ 3.82 (s, 3H), 4.83 (s, 2H), 6.92-6.94 (m, 2H), 7.33-7.38 (m, 3H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.60 (d, *J* = 2.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 44.9, 55.6, 114.8, 126.2, 127.8, 128.6, 130.7, 131.1, 132.8, 132.9, 135.1, 151.1, 159.0, 165.2.



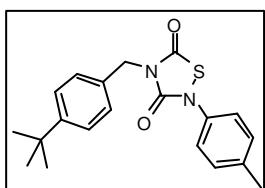
2-(3,4-dichlorophenyl)-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S32):

Yield = 26 %. ¹H NMR (400 MHz, CDCl₃) δ 4.84 (s, 2H), 7.32-7.36 (m, 2H), 7.42-7.49 (m, 2H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.70 (d, *J* = 2.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 45.1, 122.1, 124.9, 128.6, 130.9, 131.0, 131.1, 132.99, 133.05, 133.6, 134.6, 134.9, 150.5, 164.0.



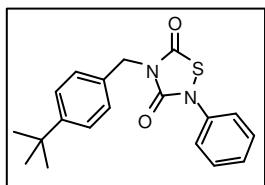
2-(4-methylbenzyl)-4-(3,4-dichlorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (S33):

Yield = 35 %. ¹H NMR (400 MHz, CDCl₃) δ 2.36 (s, 3H), 4.73 (s, 2H), 4.77 (s, 3H), 7.16-7.18 (m, 4H), 7.29 (dd, *J* = 2.1, 8.2 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 2.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 21.2, 44.7, 48.7, 128.4, 129.0, 129.3, 129.8, 130.7, 130.9, 131.2, 132.7, 132.9, 135.2, 139.0, 152.7, 165.8.



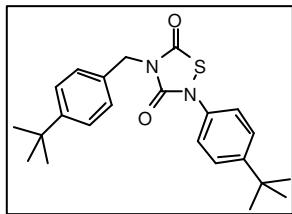
2-p-tolyl-4-(4-t-butylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S34):

Yield = 72 %. ¹H NMR (400 MHz, CDCl₃) δ 1.31 (s, 9H), 2.35 (s, 3H), 4.87 s, 2H), 7.19-7.21 (m, 2H), 7.36-7.38 (m, 4H), 7.43-7.45 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 31.3, 34.6, 45.8, 123.7, 125.7, 128.9, 130.0, 132.2, 133.2, 137.2, 151.2, 151.4, 165.2.



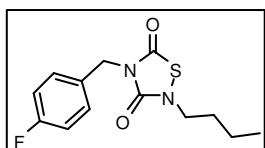
2-phenyl-4-(4-t-butylbenzyl)-1,2,4-thiadiazolidine-3,5-dione (S35):

Yield = 81 %. ¹H NMR (400 MHz, CDCl₃) δ 1.31 (s, 9H), 4.88 (s, 2H), 7.25-7.29 (m, 1H), 7.36-7.45 (m, 6H), 7.50-7.52 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 31.3, 34.6, 45.9, 123.4, 125.7, 126.9, 128.9, 129.5, 132.1, 135.9, 151.1, 151.4, 165.0.



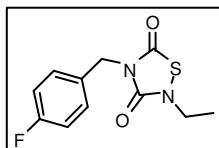
**2-(4-*t*-butylphenyl)-4-(4-*t*-butylbenzyl)-1,2,4-thiadiazolidine-3,5-dione
(S36):**

Yield = 62 %. ^1H NMR (400 MHz, CDCl_3) δ 1.30 (s, 9H), 1.31 (s, 9H), 4.88 (s, 2H), 7.36-7.38 (m, 2H), 7.41-7.42 (m, 4H), 7.43-7.45 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 31.2, 31.3, 34.6, 34.7, 45.8, 123.4, 125.7, 126.5, 129.0, 132.1, 133.0, 150.4, 151.2, 151.4, 165.3.



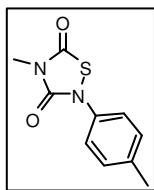
2-butyl-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (9a):

Yield = 65 %. ^1H NMR (400 MHz, CDCl_3) δ 0.94 (t, J = 7.4 Hz, 3H), 1.31-1.40 (m, 2H), 1.57-1.64 (m, 2H), 3.61 (t, J = 7.2 Hz, 2H), 4.78 (s, 2H), 6.98-7.02 (m, 2H), 7.41-7.44 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.4, 19.5, 30.6, 44.7, 45.1, 115.5 (d, J = 21.5 Hz), 130.8 (d, J = 8.3 Hz), 131.1 (d, J = 3.3 Hz), 152.8, 162.6 (d, J = 247.0 Hz), 165.9.



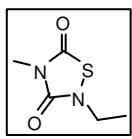
2-ethyl-4-(4-fluorobenzyl)-1,2,4-thiadiazolidine-3,5-dione (9b):

Yield = 72 %. ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, J = 7.2 Hz, 3H), 3.70 (q, J = 7.2 Hz, 2H), 4.80 (s, 2H), 7.01-7.05 (m, 2H), 7.44-7.47 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 40.1, 45.2, 115.6 (d, J_{CF} = 21.1 Hz), 130.9 (d, J_{CF} = 8.0 Hz), 131.2 (d, J_{CF} = 3.0 Hz), 152.7, 162.7 (d, J_{CF} = 247.5 Hz), 165.9.



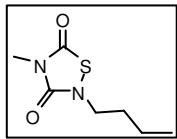
2-p-tolyl-4-methyl-1,2,4-thiadiazolidine-3,5-dione (10a):

Yield = 69 %. ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 3.29 (s, 3H), 7.10-7.12 (m, 1H), 7.21-7.24 (m, 2H), 7.36-7.38 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 28.7, 123.9, 129.6, 130.1, 133.1, 137.4, 151.4, 165.5.



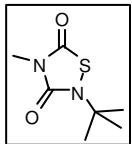
2-ethyl-4-methyl-1,2,4-thiadiazolidine-3,5-dione (10b):

Yield = 76 %. ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, J = 7.2 Hz, 3H), 3.17 (s, 3H), 3.67 (q, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 28.5, 40.1, 153.0, 166.2.



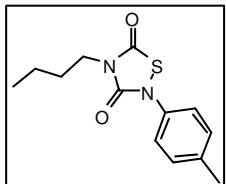
2-butyl-4-methyl-1,2,4-thiadiazolidine-3,5-dione (10c):

Yield = 75 %. ^1H NMR (400 MHz, CDCl_3) δ 0.87 (t, J = 7.3 Hz, 3H), 1.25-1.34 (m, 2H), 1.51-1.58 (m, 2H), 3.11 (s, 3H), 3.55-3.58 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.3, 19.3, 28.2, 30.5, 44.4, 153.0, 165.9.



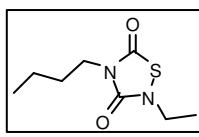
2-*t*-butyl-4-methyl-1,2,4-thiadiazolidine-3,5-dione (10d):

Yield = 90 %. ^1H NMR (400 MHz, CDCl_3) δ 1.55 (s, 9H), 3.14 (s, 3H). ^{13}C NMR (100 Hz, CDCl_3) δ 28.0, 28.6, 59.1, 152.5, 166.1.



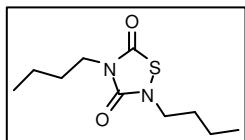
2-*p*-tolyl-4-butyl-1,2,4-thiadiazolidine-3,5-dione (11a):

Yield = 75 %. ^1H NMR (400 MHz, CDCl_3) δ 0.97 (t, $J = 7.4$ Hz, 3H), 1.35-1.45 (m, 2H), 1.68-1.75 (m, 2H), 2.35 (s, 3H), 3.74-3.78 (m, 2H), 7.20-7.22 (m, 2H), 7.37-7.39 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.6, 19.9, 21.0, 29.8, 42.7, 123.7, 130.1, 133.3, 137.1, 151.3, 165.3.



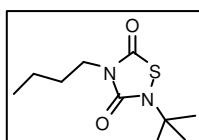
2-ethyl-4-butyl-1,2,4-thiadiazolidine-3,5-dione (11b):

Yield = 75 %. ^1H NMR (400 MHz, CDCl_3) δ 0.92 (t, $J = 7.4$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.29-1.38 (m, 2H), 1.60-1.67 (m, 2H), 3.64-3.69 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.5, 13.7, 19.8, 29.7, 39.9, 42.4, 153.0, 166.0; anal. ($\text{C}_8\text{H}_{14}\text{N}_2\text{O}_2\text{S}$); CHN



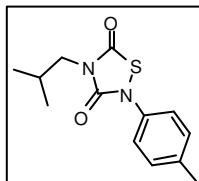
2,4-dibutyl-1,2,4-thiadiazolidine-3,5-dione (11c):

Yield = 72 %. ^1H NMR (400 MHz, CDCl_3) δ 0.93 (t, $J = 7.4$ Hz, 3H), 0.94 (t, $J = 7.4$ Hz, 3H), 1.29-1.40 (m, 4H), 1.57-1.69 (m, 4H), 3.61 (t, $J = 7.2$ Hz, 2H), 3.66 (t, $J = 7.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.5, 13.6, 19.6, 19.9, 29.8, 30.7, 42.5, 44.6, 153.2, 166.1.



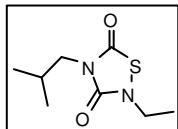
2-*t*-butyl-4-butyl-1,2,4-thiadiazolidine-3,5-dione (11d):

Yield = 70 %. ^1H NMR (400 MHz, CDCl_3) δ 0.94 (t, $J = 7.4$ Hz, 3H), 1.32-1.39 (m, 2H), 1.54 (s, 9H), 1.59-1.67 (m, 2H), 3.63 (t, $J = 7.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.6, 19.9, 28.5, 29.8, 42.0, 59.1, 152.5, 166.0.



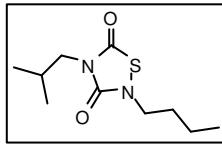
2-*p*-tolyl-4-isobutyl-1,2,4-thiadiazolidine-3,5-dione (12a):

Yield = 65 %. ^1H NMR (400 MHz, CDCl_3) δ 0.97 (s, 3H), 0.99 (s, 3H), 2.16-2.23 (m, 1H), 2.36 (s, 3H), 3.59 (d, $J = 7.4$ Hz, 2H), 7.21-7.23 (m, 2H), 7.37-7.39 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 20.0, 21.0, 27.2, 49.9, 123.7, 130.1, 133.3, 137.2, 151.5, 165.6.



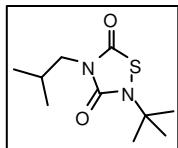
2-ethyl-4-isobutyl-1,2,4-thiadiazolidine-3,5-dione (12b):

Yield = 70 %. ^1H NMR (400 MHz, CDCl_3) δ 0.90 (s, 3H), 0.92 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 2.08-2.15 (m, 1H), 3.47 (d, J = 7.5 Hz, 2H), 3.67 (q, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.7, 19.8, 27.1, 39.9, 49.6, 153.2, 166.2.



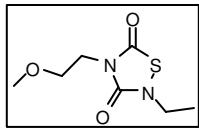
2-butyl-4-isobutyl-1,2,4-thiadiazolidine-3,5-dione (12c):

Yield = 73 %. ^1H NMR (400 MHz, CDCl_3) δ 0.92 (s, 3H), 0.94 (s, 3H), 0.95 (t, J = 7.3 Hz, 3H), 1.35-1.40 (m, 2H), 1.59-1.66 (m, 2H), 2.11-2.18 (m, 1H), 3.50 (d, J = 7.5 Hz, 2H), 3.63 (t, J = 7.20 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.5, 19.6, 19.8, 27.2, 30.7, 44.6, 49.7, 153.4, 166.3.



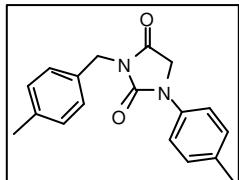
2-t-butyl-4-isobutyl-1,2,4-thiadiazolidine-3,5-dione (12d):

Yield = 68 %. ^1H NMR (400 MHz, CDCl_3) δ 0.91 (s, 3H), 0.93 (s, 3H), 1.55 (s, 9H), 2.07-2.18 (m, 1H), 3.46 (d, J = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 19.9, 27.2, 28.5, 49.2, 59.1, 152.8, 166.2.



2-ethyl-4-(2-methoxyethyl)-1,2,4-thiadiazolidine-3,5-dione (13):

Yield = 70 %. ^1H NMR (400 MHz, CDCl_3) δ 1.25 (t, J = 7.2 Hz, 3H), 3.34 (s, 3H), 3.60 (t, J = 5.6 Hz, 2H), 3.67 (q, J = 7.2 Hz, 2H), 3.86 (t, J = 5.6 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.7, 40.0, 41.6, 58.6, 68.6, 152.8, 166.1; anal. ($\text{C}_7\text{H}_{12}\text{N}_2\text{O}_3\text{S} \cdot 1/2\text{H}_2\text{O}$); CHN



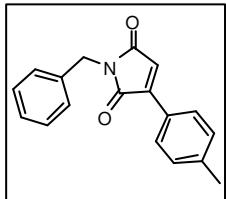
3-(4-methylbenzyl)-1-p-tolylimidazolidine-2,4-dione (14):

Ethyl bromoacetate (4.0 g, 30.0 mmol) was added to a solution of *p*-toluidine (2.1 g, 20 mmol) and sodium acetate (2.1 g, 26 mmol) in ethanol (26 mL). The resulting solution was warmed to 80 °C and stirred for 1 h before being cooled to room temperature. The reaction was quenched with water (20 mL) and the aqueous fraction extracted with ethyl acetate (3 x 20 mL). The organic fractions were combined, dried (MgSO_4) and filtered, and the solvent was removed under reduced pressure. Silica chromatography (0-20% ethyl acetate/hexane) provided ethyl 2-(*p*-tolylamino)acetate as a pale oil (1.9 g, 50%). Ethyl 2-(*p*-tolylamino)acetate (260 mg, 1.4 mmol) was dissolved in toluene (5 mL). Methyl benzylisocyanate (200 mg, 1.4 mmol) was added to this solution. The mixture was heated to reflux and stirred for 5 h, until TLC analysis demonstrated that the reaction was complete. The reaction mixture was then cooled to room temperature, and the solvent was removed under reduced

pressure. Silica chromatography (0-20% ethyl acetate/hexane) provided ethyl 2-[3-(4-methylbenzyl)-1-*p*-tolylureido]acetate as a pale oil (455 mg, 98%).

Ethyl 2-[3-(4-methylbenzyl)-1-*p*-tolylureido]acetate (455 mg, 1.3 mmol) was dissolved in THF (10 mL) and added dropwise to a solution of NaH (68 mg, 2.8 mmol) in THF (10 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature slowly and stirred for 18 h before the reaction was quenched with water (5 mL). The aqueous fraction was then extracted with dichloromethane (3 x 20 mL). The organic fractions were combined, dried (MgSO_4), and filtered, and the solvent was removed under reduced pressure. Column chromatography (0-20% ethyl acetate/hexane) provided **14** as a white solid.

Yield = 93 %. ^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 6H), 4.25 (s, 2H), 4.71 (s, 2H), 7.13-7.15 (m, 2H), 7.16-7.18 (m, 2H), 7.36-7.38 (m, 2H), 7.40-7.43 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 20.7, 21.1, 42.4, 50.0, 118.5, 129.0, 129.4, 129.8, 132.9, 134.2, 135.0, 137.9, 154.1, 168.2.



1-benzyl-3-*p*-tolyl-1*H*-pyrrole-2,5-dione (15):

A solution of bromomaleic anhydride (1 g, 5.7 mmol) and benzyl amine (0.7 mL, 6.8 mmol) in acetic acid (15 mL) was warmed to 50 °C and stirred overnight. The reaction was then cooled to room temperature, diluted with CH_2Cl_2 (50 mL) and washed with NaHCO_3 (3 x 25 mL) and brine (25 mL). The organic layer was then dried (MgSO_4), filtered and the solvent removed under reduced pressure. The residue was purified using gradient flash chromatography (0-100% ethyl acetate in pet ether) to provide 1-benzyl-3-bromo-1*H*-pyrrole-2,5-dione (**18**). ^1H NMR (400 MHz, CDCl_3) δ 4.71 (s, 2H), 6.87 (s, 2H), 7.26-7.37 (m, 5H).

A stirred solution of 1-benzyl-3-bromo-1*H*-pyrrole-2,5-dione (0.26 g, 1.0 mmol) and *p*-tolylboronic acid (0.16 g, 1.2 mmol) in dioxane (10 mL) was degassed with a stream of nitrogen for 10 minutes before being treated with CsF (0.39 g, 2.6 mmol) and $\text{Cl}_2\text{Pd}(\text{dpff})\cdot\text{CH}_2\text{Cl}_2$ (0.05 g, 0.06 mmol). The reaction was stirred at room temperature for 1 h then warmed to 40 °C for 1 h. The mixture was then cooled, diluted with CH_2Cl_2 (30 mL) and filtered through a pad of celite. The filtrate was concentrated under reduced pressure and purified using gradient flash chromatography (0-10% ethyl acetate in pet ether) to provide the title compound **15**.

^1H NMR (400 MHz, CDCl_3) δ 2.40 (s, 3H), 4.73 (s, 2H), 6.68 (s, 1H), 7.24-7.34 (m, 5H), 7.38-7.40 (m, 2H), 7.82-7.84 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.6, 41.6, 122.7, 126.0, 127.8, 128.5, 128.6, 128.7, 129.7, 136.5, 141.8, 143.9, 170.2, 170.6.

Reaction of **1a with propanethiol**

An NMR sample was prepared containing **1a** (15 mg, 0.05 mmol) and propanethiol (8 μ L, 0.1 mmol) in CDCl_3 (0.8 mL). Proton NMR spectrum were run at intervals, and complete consumption of **1a** was observed after 5 days. The solvent was then removed under reduced pressure to remove excess propanethiol and the sample redissolved in CDCl_3 for further analysis.

^1H NMR (400 MHz, CDCl_3) δ 1.00 (t, $J = 7.3$ Hz, 3H), 1.64-1.69 (m, 2H), 2.31 (s, 3H), 2.76 (t, $J = 7.1$ Hz, 2H), 5.16 (s, 2H), 6.99-7.04 (m, 2H), 7.12-7.14 (m, 2H), 7.30-7.34 (m, 2H), 7.39-7.41 (m, 2H), 10.69 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 12.9, 20.7, 22.0, 40.9, 46.9, 115.5 (d, $J = 22$ Hz), 120.5, 122.5, 128.9 (d, $J = 8.0$ Hz), 129.5, 129.9, 132.0 (d, $J = 3.0$ Hz), 134.2, 134.6, 150.4, 162.2 (d, $J = 246.3$ Hz), 172.9.